Summary of Safety and Effectiveness Data

The Eclipse PMR Holmium Laser System

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Eclipse PMR Holmium Laser System

Eclipse Surgical Technologies, Inc.

1. General Information

Device Generic Name:.....Percutaneous Myocardial Revascularization (PMR) device

Device Trade Name:.....Eclipse PMR Holmium Laser System

Includes:

New Star Holmium Laser
Axcis Laser Catheter
Axcis Aligning Catheter
Ivy ECG Monitor

Applicant's Name and Address:.....Eclipse Surgical Technologies, Inc.
1049 Kiel Court
Sunnyvale, CA 94089

PMA Application Number:..... P970029/S004

Date of Panel Recommendation: .....

Date of Notice of Approval to the Applicant:

2. Indications and Usage

The Eclipse PMR System is indicated for use in percutaneous myocardial revascularization (PMR) procedures to decrease angina and increase exercise tolerance in patients with chronic angina (Canadian Cardiovascular Society Angina Scale Class III or IV) which is refractory to medical treatment and secondary to objectively demonstrated coronary artery disease and with a region of the myocardium with reversible ischemia not amenable to direct coronary revascularization.

3. Contraindications

No contraindications known.

4. Warnings and Precautions

See WARNINGS AND PRECAUTIONS in the final draft labeling (Instructions for Use) for a complete list. Precautions to be followed during the PMR procedure include, but are not limited to:

- The Eclipse PMR System should only be used by properly trained cardiologists.
- The wall thickness in the targeted region should be assessed prior to the PMR procedure using echocardiography. PMR should not be performed in areas of the myocardium that are:
  - Less than 8 mm in wall thickness
  - Infarcted
  - In the region of the mitral valve, mitral valve apparatus, or papillary muscle
  - In the region of a left ventricular mural thrombus
- PMR should only be performed under fluoroscopic observation and care must be taken not to duplicate channel locations since firing into a previously formed channel may cause perforation.
- If the patient experiences ventricular fibrillation during the procedure, the procedure should be discontinued and the arrhythmia treated as appropriate. A defibrillator should be readily available at all times.

5. Device Description

The Eclipse PMR Holmium Laser System is composed of the New Star Holmium: YAG laser, laser energy delivery system and ECG monitor. The laser radiation emitted from this system has a wavelength of approximately 2.1 microns, which is in the mid-infrared (invisible) range of the electromagnetic spectrum. Water is the target absorber for this laser wavelength. This laser emits 350 microsecond laser radiation pulses at a 35 millisecond pulse repetition interval. The energy output from the laser aperture is 2.7 Joules while the clinical level is 2 Joules per pulse. The pulses are synchronized with the cardiac cycle through the ECG monitor which provides a trigger signal to allow synchronization of the heartbeat with the delivery of laser energy. There is a visible laser beam used for calibration.

The laser energy is delivered to the target tissue via an optical fiber. The Axcis PMR Delivery System has been designed for this purpose and consists of the Axcis Laser Catheter and the Axcis Aligning Catheter. The Axcis Laser Catheter contains a single solid core optical fiber of approximately 365 micron diameter terminated with a quartz lens surrounded by 4 penetration-depth limiting nitinol petals at the distal end and contained within a catheter shaft of braided PEBAX. A gold marker band is present at the distal end to facilitate fluoroscopic visualization of the catheter. A stainless steel Introducer Tool is used to fold the petals forward prior to insertion of the Laser Catheter into the Aligning Catheter. Rotation, advancement and retraction of the

catheter is controlled with the proximal controller portion of the device. The Axcis Aligning Catheter is an approximately 9 French braid-reinforced catheter with a soft distal tip. The distal portion comes in 5 configurations to access various shaped ventricles.

6. Alternative Practices or Procedures

PMR is intended to treat a group of patients who are not candidates for alternative interventions. PMR is a non-surgical, percutaneous approach to the heart. The only alternative practices for preventing, curing, or mitigating the symptoms which PMR is intended to treat in this subset of angina patients are maximal anti-anginal medication and TMR, a surgical approach to revascularize the heart.

7. Marketing History

These devices have not been marketed in the United States. The following devices have received the CE mark:

New Star Holmium Laser
Axcis Laser Catheter
Axcis Aligning Catheter
Ivy ECG Monitor

The Eclipse PMR System has been marketed in the following countries: Germany, The Netherlands, Italy, Spain, Austria, the United Kingdom, Switzerland, Norway, India, China, and Canada. Axcis Aligning Catheters from lots manufactured after February 1999 were voluntarily recalled by Eclipse in February 2001 for delamination of the inner lining which was not associated with any adverse events. Two lots of Axcis Laser Catheters were voluntarily recalled by Eclipse in April 1999 due to three instances of lens separation during procedures. There were no clinical sequellae as a result of these events.

8. Adverse Events

8.1 Observed Adverse Events

The randomized trial of PMR, the PACIFIC Study, compared PMR plus medication (PMR+MEDs) with medication alone (MEDs) and enrolled 200 subjects who were studied for an average of 11.1 months.

There were no intra-procedural deaths in the study. Within 30 days of treatment, one PMR+MEDs patient died of cardiac causes. During 12 months follow-up an additional six PMR+MEDs patients died (5 from cardiac causes and 1 respiratory arrest) and 2 subjects in the MEDs group died (both due to cardiac causes).

Serious adverse events which occurred in the study are summarized in **Table 1**.

Table 1: Serious Adverse Events* in the PACIFIC PMR Randomized Trial

Includes all adverse events, both related and unrelated to PMR, sorted by system affected.

	PMR+MEDs (n=100)		MEDs (n=100)	
Event[1]	**Patients with Event**	**Number of Events**	**Patients with Event**	**Number of Events**
All CV events combined	50	108	48	103
Angina	25	49	39	74
Arrhythmias[2]	11	12	4	6
Death (all causes)	7	7	2	2
Heart Failure	8	8	2	2
Injury to heart structure (perforation)	3	3	0	0
Myocardial infarction	11	12	5	8
Other cardiovascular[3]	16	18	7	9
Thromboembolic disorder	4	4	2	3
All DER Events Combined	1	1	2	3
All GU Events Combined	2	2	2	2
All GEN Events Combined	10	11	7	7
All GI Events Combined	8	12	3	4
All NEU Events Combined	3	4	1	1
All PSY Events Combined	2	2	1	2
All RES Events Combined	7	10	3	4
All AE Combined	56	159	52	130

[1]Abbreviations: CV = cardiovascular, DER = dermatologic, GEN = general, GI = gastrointestinal, GU = genitourinary, HEM = hematologic, LAB = laboratory, MET = metabolic, MUS = musculoskeletal, NEU = neurologic, PSY = psychiatric, RES = respiratory, AE = adverse events.

[2]Arrhythmias (number of patients with each in treatment/control groups) were: arrhythmia (0/2), ventricular arrhythmia (1/0), AV block complete (1/0), bradycardia (4/1), atrial fibrillation (2/0), atrial flutter (2/0), heart block (1/0), tachycardia (0/1).

[3]Other cardiovascular events (number of patients with each in treatment/control groups) were: heart arrest (4/0), syncope (2/2), vascular disease peripheral (3/2), amblyopia (0/1), vascular anomaly (1/0), cellulitis (1/0), creatine PK increase (1/0), pericardial effusion (1/0), embolism (1/0), hypotension (1/0), artery occlusion (0/1), carotid occlusion (0/1), coronary stenosis (1/0), ulcer (1/0).

8.2 Potential Adverse Events

Adverse events potentially associated with the use of PMR but not observed in the study include (in alphabetical order):

Allergic reaction to contrast reagent

Arterial dissection

Bleeding

Cardiogenic shock

Fragmented catheters and lens tip

Left ventricular dysfunction

Renal insufficiency

Vascular damage

9. Summary of Pre-Clinical Studies

9.1 Biocompatibility Testing

All patient contacting components of the fiberoptic delivery system underwent biocompatibility testing in accordance with FDA General Program Memorandum #G95-1, which provides an FDA-modified matrix of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing." The Introducer Tool is composed of stainless steel, which is a known biocompatible material. **Table 2** summarizes the biocompatibility tests conducted and the results. Test results demonstrate that all devices are biocompatible for their intended use.

Table 2: Summary of Axcis PMR Delivery System Biocompatibility Testing

Test	Results
Cytotoxicity	System was non-cytotoxic.
Sensitization	System did not cause delayed dermal contact sensitization.
Intracutaneous Reactivity	System did not cause significant irritation or toxicity.
Systemic Toxicity	System was not toxic systemically and did not cause mortality.
Hemolysis	System was non-hemolytic.
Complement Activation	System activated 14% of the normalized positive control result.*
Thrombogenicity	System exhibited minimal thrombogenicity.
Pyrogenicity	System was non-pyrogenic.

* Test report notes that all biomaterials activate complement to some extent and that an acceptable level has not yet been established.

9.2 Sterility Testing

The Axcis Laser Catheter and Axcis Aligning Catheter are single-use devices which are provided pre-sterilized to the user. These devices are sterilized using an ethylene oxide (EtO) cycle. The Introducer Tool is a reusable device which is sterilized by the hospital, using a recommended steam autoclave cycle. The sterilization cycles were validated to ensure successful sterilization to a Sterility Assurance Level (SAL) of 10^{-6}. **Table 3** summarizes the sterilization validations performed.

Table 3: Summary of Sterility Testing

Device	Validation Test Method	Test Results
Axcis Laser Catheter & Axcis Aligning Catheter	Testing was performed using the biological indicator overkill method. The following residual levels were measured: ethylene oxide (EtO), ethylene chlorohydrin (ECH) and	Devices met the SAL acceptance criteria. All residual levels met the FDA acceptance criteria. Testing demonstrated that the devices can be successfully sterilized using the

	ethylene glycol (EG).	specified EtO cycle.
Introducer Tool	Testing was performed using the biological indicator overkill method.	Devices met the SAL acceptance criteria. Testing demonstrated that the devices can be successfully sterilized using the specified gravity or prevacuum steam sterilization methods.

In addition, cleaning evaluation studies were performed with the Introducer Tool to validate procedures for cleaning the device prior to sterilization and re-use.

Shelf Life Studies

Twenty-four month accelerated aging studies were performed on the Axcis Laser Catheter and Axcis Aligning Catheter devices. These studies demonstrated that sterility, package integrity, and product functionality is maintained for a minimum of 24 months. Based upon these results, a shelf life of two years has been established for these devices.

9.3 Catheter Functionality Testing

In vitro testing was performed with the Axcis Laser Catheter and Axcis Aligning Catheter devices to demonstrate that they function as intended and meet the requirement of FDA "Guidance for the Submission of Research and Marketing Application for Interventional Cardiology Devices (May 1993)".

The Axcis Laser Catheter was tested to assess the mechanical integrity, optical integrity and functionality of the device. The sequence of tests was designed to provide a baseline quality assessment followed by clinical simulation challenge tests and post challenge assessment. Challenge tests included Repeated Introduction, Repeated Laser Firing in Saline, Channel Creation in Porcine Heart, Repeated Flexion of the Distal Lens Assembly and Torque and Rotational Control. The effects of the challenge tests on the device were monitored by Visual Inspection, Optical Energy Transmission, Tip Temperature, and Spatial Output Measurement tests. Devices were also subjected to final destructive tests. The results of the *in vitro* tests demonstrated that the Laser Catheters performed according to the specified acceptance criteria for the tests.

The Axcis Aligning Catheters were tested to ensure functionality of torque and rotational control functions and ability to maintain flow rates. Tests included Dimensional and Visual Inspections, Repeated Introduction, Torque and Rotational Control, Tip Shape Retention, and Sustained Pressurization. Aligning Catheters were also tested by Peak Pressure at Failure and destructive Torque and Tensile testing. The results of the *in vitro* tests demonstrated that the Aligning Catheters performed according to the specified acceptance criteria for the tests.

The Axcis PMR Delivery System was tested *in vivo* in the porcine model to characterize acute and chronic physiologic responses to the creation of endocardial channels. Results demonstrated that endocardial channels were histologically similar to the transmural channels created using a

surgical approach to the heart. The safety of the device in the porcine model was demonstrated by the lack of arrhythmic events and lack of long term effect on myocardial function.

9.4 Laser Functionality Testing

9.4.1 Electrical Safety Testing

An independent laboratory evaluated the electrical safety of the New Star laser. The New Star laser was tested and was found to be in compliance with IEC 601-1/EN60601, the European standard for general safety requirements for medical electrical equipment, and IEC 601-2-22/EN 60601-2-22, the European standard for particular requirements for laser equipment. As part of meeting the IEC 601-2-22 standard, the New Star laser was also found to be in compliance with IEC 601-1-2, the European electromagnetic compatibility immunity standard. In addition, the New Star laser was tested for, and was found to be in compliance with, EN 55011 for Group I, Class A, 1991 the European electromagnetic interference standard for conducted emissions and radiated emissions.

9.4.2 Software Validation

The New Star laser software was validated by testing the error codes according to safety, functional performance and software architectural specification. Where appropriate, tests were performed with the Axcis PMR Delivery System devices. All portions of the test were completed successfully.

9.4.3 Laser Reliability

Reliability and life testing was performed for the New Star laser. There were no failures of the laser during the life test and the reliability testing significantly exceeded the requirement.

9.4.4 Environmental Validation

Environmental testing was performed and demonstrated compliance of the New Star laser with the environmental requirements. The devices were tested and found to maintain sterile barrier properties after testing.

9.5 ECG Monitor Functionality Testing

9.5.1 Electrical Safety Testing

The ECG monitor was tested by the manufacturer, Ivy Biomedical, Branford CT and found to meet the requirements of EN55011 for Group I, Class A, 1991 for conducted emissions and radiated emissions. The monitor complies with EN 61000-4-2, 1995-01, electrostatic discharge immunity; EN 61000-4-3 1995-02, radiated electromagnetic immunity; EN 61000-4-4 1995-01 electrical fast transient/burst immunity and EN 50141 1994 conducted disturbance induced by RF fields.

9.5.2 Software Validation

The software for the ECG monitor was validated and found to perform within specifications.

9.5.3 Reliability Testing

The ECG delayed trigger function used to synchronize the heartbeat with the delivery of laser energy was tested and the results demonstrated that the trigger position displayed on the monitor corresponded to the actual trigger output. In addition, testing demonstrated that the ECG monitor reliably produced a trigger pulse and that the laser was reliably triggered by the signal produced by the monitor.

9.6 Shipping Validation

The shipping validation for the New Star Laser was performed according to ASTM D4169 Distribution Cycle 12, Assurance Level 1. All test results passed the required ASTM standards with no exceptions. Shipping and handling tests of the Laser Catheter and Aligning Catheters were conducted per the requirements of ASTM D4169, Distribution Cycle 13, Assurance Level 1. The results validated the integrity of the packaging and the functionality of the devices after testing. More than 20,000 ECG units have been shipped with no history of problems with the packaging.

10. Summary of Clinical Studies

The Eclipse PMR Holmium Laser System was evaluated in a prospective, randomized, controlled trial, the PACIFIC Study, which compared PMR plus medication (PMR+MEDs) with medication alone (MEDs). A total of 200 patients were enrolled in the study between November 1997 and August 1998. The study ended in August 1999 when the final 12 month follow-up visits were completed.

10.1 Study Design

The PACIFIC multi-center, prospective, randomized controlled trial was conducted at 11 U.S. sites. The study was conducted in patients with Canadian Cardiovascular Society class III or IV angina, ejection fraction $\geq$30%, and an area of reversible ischemia, who were not candidates for other interventions. Patients were excluded from the study if they had had a Q wave MI within the previous 3 months or a non-Q wave MI within the previous 6 weeks, if they had heart failure requiring a dose of diuretic equivalent to >80 mg Lasix per day, had clinically significant ventricular arrhythmias, left ventricular thrombus, aortic valve stenosis with valve area $<1.5cm^2$, myocardial wall thickness less than 8 mm in the area intended for treatment, a significant change in oral anti-anginal medication within the 14 days prior to treatment or hospitalization for unstable angina. Other exclusions from the study were persons with significant alterations in angina pattern or clinical status since the last coronary angiogram, cardiac transplant, inability to perform exercise tolerance testing without significant risk, failure to experience angina during testing, baseline renal insufficiency, severe peripheral vascular disease, impaired fluoroscopic visualization for any reason, and those who were poor candidates for interventional cardiac procedures.

The objectives of the study were to evaluate whether the Eclipse PMR System, when used to create small channels into the myocardium, could provide improvement at 12 months in Canadian Cardiovascular Society Angina Scale (CCSAS) classification and Exercise Tolerance Test (ETT) results. The secondary endpoint was improvement in quality of life as measured by the Seattle Angina Questionnaire.

10.2 Patient Description and Accountability

Patients were randomized into the study between November 1997 and August 1998 at 11 United States centers. Patients were randomly assigned to the two treatment groups: 100 to percutaneous myocardial revascularization plus medical management (PMR+MEDs) and 100 to medical management (MEDs). There were 200 patients randomized into the study and there were 17 withdrawals and 9 deaths. All of the remaining 174 patients reached the one year follow-up time point. The patient baseline characteristics and cardiac risk factors are described in **Table 4**.

Table 4: Patient Baseline Characteristics and Cardiac Risk Factors

	PMR+MEDs	MEDs	P Value
n patients =	100	100	
Male	84% (84)	86% (86)	0.843
Female	16% (16)	14% (14)	
Age (Years)			
Mean ? SD	63 ? 9.4	62 ? 10.1	0.554
Range {Min, Max}	[39, 83]	[38, 90]	
Pre Ejection Fraction (%)			
Mean ? SD	51 ? 9.9	51 ? 8.6	0.933
History of Diabetes	49% (49)	43% (43)	0.478
History of Smoking			0.754
Never	28% (28)	23% (23)	
Current	11% (11)	11% (11)	
Former	61% (61)	66% (66)	
History of Hypertension	69% (69)	79% (79)	0.146
History of Hyperlipidemia	70% (70)	88% (88)	0.003
Family History of CAD	65% (65)	76% (76)	0.038
History of MI	64% (64)	68% (68)	0.654
Previous PTCA	9% (9)	7% (7)	
Previous CABG	35% (35)	38% (38)	0.076
History of both PTCA and CABG	42% (42)	51% (51)	

10.3 Results

10.3.1 Procedure Description and Data

PMR was performed using a percutaneous access route typical of other interventional cardiac procedures. The Laser Catheter containing the fiber optic was introduced through the Aligning Catheter and used to apply laser energy to the endocardial surface of the left ventricle. As the fiber was advanced, pulsed laser energy was delivered to the myocardium to a create channels with a depth of 6-8 mm. PMR channels were placed approximately 1 cm apart using fluoroscopic visualization for catheter placement. The laser was synchronized to fire at the electrocardiographic R-wave, when the left ventricle was at maximum contractile width.

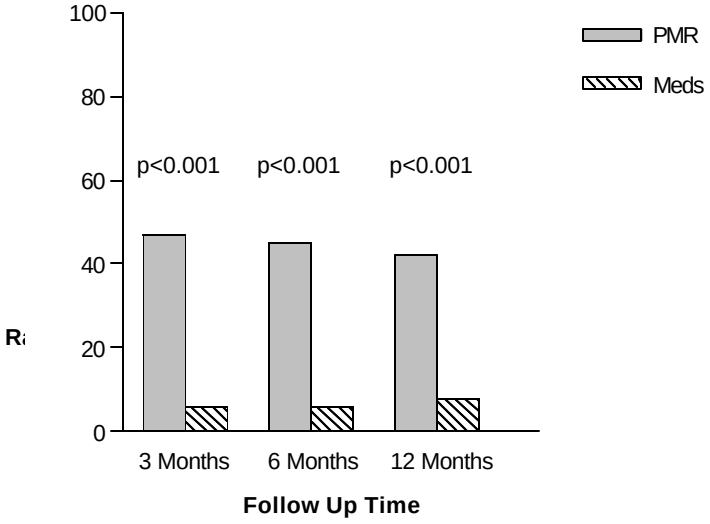
The number of PMR channels created during the procedure ranged from 8 to 35 (mean 16.1), using an energy of 2 Joules per pulse.

There were no intra-procedural deaths. Within 30 days of PMR, 1 patient died of cardiac causes. There were no deaths in the control group within 30 days of enrollment.

10.3.2 Primary Outcome Measures

Angina Improvement: Angina improvement was defined as improvement in angina symptoms from baseline by at least 2 angina classes, based on the Canadian Cardiovascular Society definition of angina. All patients had Class III or IV angina at baseline. **Figure 1** shows the percent of patients who had angina improvement at 3, 6 and 12 months follow-up. At each follow-up time point, a significantly larger percent of PMR+MEDs patients experienced angina improvement than MEDs patients.

Figure 1: Angina Improvement at 3, 6 and 12 months*



	PMR+MEDS	MEDs	P-value
Baseline Class III **Class IV**	62.0% (n = 62) 38.0% (n = 38)	62.0% (n = 62) 38.0% (n = 38)	1.000
3 Months **Success**	47.0% (n = 47)	6.0% (n = 6)	<0.001
6 Months **Success**	45.0% (n = 45)	6.0% (n = 6)	<0.001
12 Months **Success**	42.0% (n = 42)	8.0% (n = 8)	<0.001

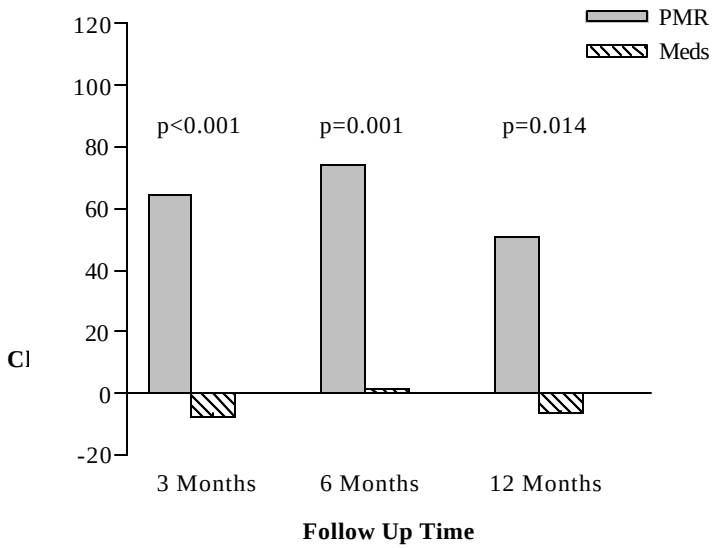
* Last observation carried forward analysis (LOCF). In this analysis values for patients who were withdrawn or had re-interventions were the values obtained at the visit prior to withdrawal or re-intevention. For patients who died the value was set at '5' (normal CCSAS specifies values of 1-4). Angina improvement is an improvement of 2 or more classes from baseline to 3, 6, or 12 months. Otherwise failure is indicated.

Angina was also assessed using a standard questionnaire administered in a blinded fashion by a clinical research organization. Responses were evaluated by an independent cardiologist. This independent assessment was introduced late in the study; consequently, the numbers of paired baseline-12 months assessments was small. The results of the independent angina assessment also

showed significantly more patients in the treated group, 51.5% (17/33), showed at least 2 CCSAS class improvement compared with the control group, 19.4% (7/36).

Exercise Tolerance Improvement: Maximal exercise tolerance times were assessed at baseline and at 3, 6 and 12 month follow-up using a standardized Modified Bruce Protocol at all sites. The results were interpreted by an independent core laboratory. **Figure 2** shows the percent of patients with improvement in total exercise duration at all follow-up time points. At each time point PMR+MEDs patients were able to exercise for a significantly greater time than MEDs patients.

Figure 2: Improvement in Total Exercise Duration at 3, 6, and 12 months*



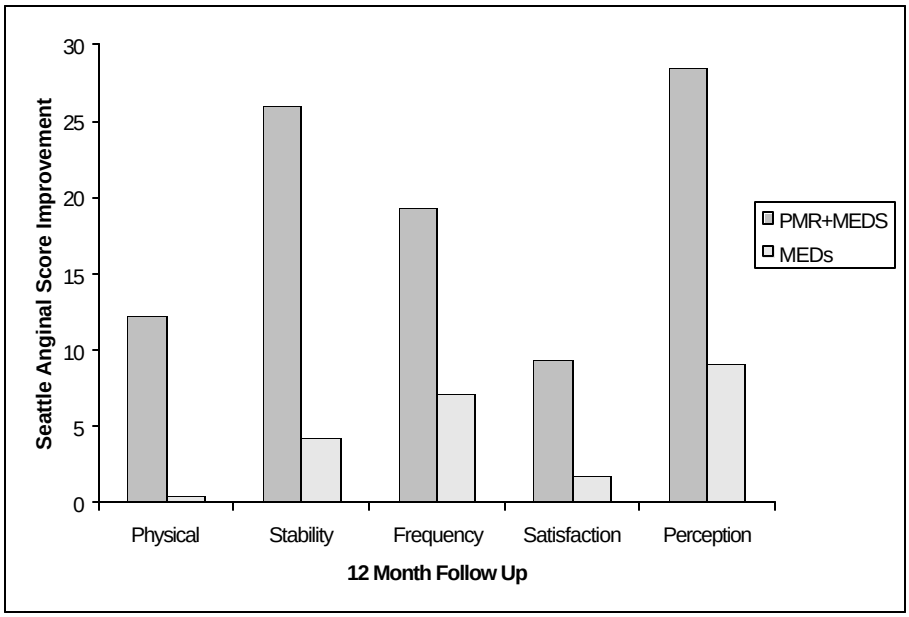
	PMR+MEDs	MEDs	P-value
Baseline	451.7 (n=99)	419.6 (n=97)	0.244
3-Month Improvement	64.1 (n=99)	-7.4 (n=95)	<0.001
6-Month Improvement	74.0 (n=99)	1.5 (n=96)	0.001
12-Month Improvement	50.8 (n=99)	-6.4 (n=97)	0.014

* Last observation carried forward analysis (LOCF). In this analysis values for patients who were withdrawn or had re-interventions were the values obtained at the visit prior to withdrawal or re-intervention. Patients who died were scored at zero minutes. Although standard exercise test protocols were created and distributed to all sites, not all subjects were tested using these protocols. Only patients using the same protocol at baseline and during follow-up evaluations were included in the final cohort for the effectiveness evaluation. Failure to use the same protocol accounts for missing data (n = <100% even with LOCF).

10.3.3 Secondary Outcome Measure

Quality of Life: Subjects were required to complete the self-administered quality of life questionnaire at baseline, 3, 6 and 12 months using the Seattle Angina Questionnaire (SAQ). The SAQ consists of 11 questions about activities that represent major aspects of physical function, including personal care, ambulation, household tasks, and recreational activities. Each answer has a weight associated with it and the weighted answers were used to derive five quality of life indices based on physical limitation, anginal stability, anginal frequency, treatment satisfaction and disease perception. The 12 month improvement in quality of life scores is illustrated in **Figure 3**. For each of the five indices, PMR+MEDs patients reported a significantly greater improvement in quality of life than the MEDs patients.

Figure 3: Improvement in Quality of Life at 12 months*



Abbreviations: Physical = Physical Limitation, Stability = Anginal Stability, Frequency = Anginal Frequency, Satisfaction = Treatment Satisfaction, Perception = Disease Perception.

Improvement	PMR+MEDs	MEDs	P-value
Physical Limitation Scale	12.3 (n=95)	0.4 (n=95)	<0.001
Anginal Stability Scale	26.0 (n=96)	4.2 (n=96)	<0.001
Anginal Frequency Scale	19.3 (n=95)	7.1 (n=97)	<0.003
Treatment Satisfaction Score	9.4 (n=96)	1.7 (n=97)	<0.001
Disease Perception/QOL Score	28.5 (n=96)	9.1 (n=97)	<0.001

* Last observation carried forward analysis (LOCF). In this analysis values for patients who were withdrawn or had re-interventions were the values obtained at the visit prior to withdrawal or re-intervention. Patients who died were scored at zero (higher scores indicate better quality of life). Missing baseline data accounts for n = <100% even with LOCF.

10.3.4 Medication Use

At 12 months follow-up, more PMR+MEDs patients decreased or remained the same in the use of anti-anginal medications compared with the MEDs patients. A higher proportion of patients in the PMR+MEDs group increased the use of diuretics compared with the MEDs group. However, changes in the use of other agents which, like diuretics, are used to treat congestive heart failure did not differ proportionally between the groups. Although the use of lipid/cholesterol regulating drugs was significantly higher in the MEDs group at baseline, changes in the use of these drugs was exactly equivalent between the two groups. Therefore, the incidence of hyperlipidemia and use of lipid/cholesterol regulators does not account for the significant improvement in angina and ETT observed in the PMR+MEDs group.

10.3.5 Morbidity and Mortality

There were no intra-procedure deaths. Within 30 days of PMR, 1 patient died of cardiac causes. During 12 months follow-up, an additional 6 patients in the PMR group died (5 due to cardiac causes and 1 due to respiratory arrest). Two patients in the MEDs group died. Kaplan-Meier analysis of the proportion of patients who died in each of the study groups did not demonstrate a difference in the risk of death associated with PMR treatment ($p = 0.17$, 2-Tail Fisher's Exact Test).

10.4 BELIEF Study Results

The **B**linded **E**valuation of **L**aser **I**ntervention **E**lectively **F**or Angina Pectoris (BELIEF Study) was a double blinded randomized study of the effects of treatment with percutaneous myocardial revascularization (PMR) plus medication compared with Sham treatment plus medication. Sham treatment was carried out in a manner in which neither the patient nor the Investigator knew which randomized treatment, PMR+MEDs or Sham+MEDs, was being implemented. The study was carried out at two investigational sites in Norway. Eclipse sponsored the study only to the extent of providing study planning and protocol design consultation and partial financial support.

The system used in the BELIEF Study, the Axcis PMR Delivery System with the New Star laser, is the same as that used in the PACIFIC trial. Moreover, the study design of the BELIEF Study was quite similar to that of the PACIFIC Study. Both were randomized studies comparing the safety and effectiveness of the Eclipse PMR System against a control; both has angina improvement as the primary endpoint; and both studies had nearly identical eligibility criteria.

At the 6 month follow-up, 64% of patients in the PMR+MEDs group improved one or more CCSAS functional classes compared with 38% n the Sham+Meds group ($p=0.02$). Additionally, significantly more patients in the PMR+MEDs group improved two or more CCSAS functional classes compared to the Sham+MEDS group (41% vs. 13% respectively; $p=0.005$). There were no significant differences between the two groups in ETT duration. Patients in the PMR group also

showed significantly better Seattle Angina Questionnaire anginal stability subscores at 6 months compared to Sham patients.

These data demonstrate that patients treated with PMR experience a significant improvement in angina symptoms compared to a Sham procedure. This double blinded randomized study demonstrates that the benefit derived from PMR is not principally due to a placebo effect. Consequently, these data demonstrate that PMR results in a dramatic improvement in angina classification in subjects with medically refractory angina who have no other treatment options.

11. Conclusions Drawn from the Studies

The preclinical studies indicate that the Eclipse PMR System has the appropriate physical and performance characteristics for its intended use as stated in the labeling.

Data from the multi-center PACIFIC Study showed that in patients with Class III or IV angina, ejection fraction $\geq$30%, and an area of reversible ischemia, who were not candidates for other interventions, percutaneous myocardial revascularization performed with the Eclipse PMR System provides significant reduction in the severity of angina and significant increase in exercise duration in patients treated with PMR compared with controls. Mortality was similar between the groups through one year.

12. Panel Recommendation

To be determined

13. FDA Decision

To be determined.

14. Approval Specifications

Directions for Use: See Final Draft Labeling (Information for Use)

Hazards to Health from Use of the Device: See INDICATIONS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE EVENTS in the labeling.

Post-approval Requirements and Restrictions

Revision History

Printed - Friday, July 06, 2001

- Eclipse internal revisions, versions 1-4
- Initial draft received from sponsor, version 4.0 May 17, 2001